compositions that include these cells.

## Support for the Amendments

Claims 1 and 24 have been amended to recite that the isolated precursor cells are multipotent. Support for these amendments is found throughout the specification (see, for example, Example 2, at pages 17-19). Claims 9, 10, and 28 have been amended to clarify that the claimed cells are differentiated cells. Support for these amendments is found at page 8, lines 8-14 of the specification. Claims 8, 11, 21, 27, 28, and 29 have been amended such that the claims are in proper form.

New claims 31-42 have been added to more clearly recite the claimed invention.

The specification teaches that precursor cells can be isolated from postnatal mammals

(Examples 1 and 2, pages 16-19), adult mammals (Example 3, pages 19-21), and humans

(Examples 13-15, page 28). No new matter has been added with these amendments.

Applicants submit that the foregoing amendments do not introduce new matter that would require the Examiner to perform additional prior art searches. First, the addition of the word "multipotent" to the claims does not broaden the claim scope, but rather restricts the claim to a subset cells recited in the previously examined claims directed to "precursor" cells. Similarly, new claims 31-42 recite that the mammal is either a postnatal mammal, an adult mammal, or a human. Each of these limitations in the newly added claims falls within the larger group (mammals) recited in the originally-examined

claims.

## Summary of the Office Action

Claim 28 is objected to under 37 CFR § 1.75(c). Claims 11, 21-23, 29, and 30 stand rejected under 35 U.S.C. § 112, first paragraph. Claim 22 stands rejected under 35 U.S.C. § 112, second paragraph. Claims 1-5, 7-11, and 21-23 stand rejected under 35 U.S.C. § 102(b). Claim 6 stands rejected under 35 U.S.C. § 103(a).

#### Rejections under 37 CFR § 1.75(c)

Claim 28 stands objected to under 37 CFR 1.75(c) as being of improper dependent form. This objection has been overcome by amendment to claim 28, which is now dependent on claim 27.

# Rejections under 35 U.S.C. § 112, first paragraph

Claims 11, 21-23, 29, and 30 are rejected for containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to make or use the invention. This rejection has been met by amendment of claims 11, 21, and 29, cancellation of claims 22, 23, and 30.

### Rejections under 35 U.S.C. § 112, second paragraph

Claim 22 is rejected for indefiniteness. The Examiner stated that the phrase "testing toxicity" is unclear. Claim 22 has been canceled, and this rejection can now be withdrawn.

## Rejections under 35 U.S.C. § 102(b)

<u>Calof</u>

Claims 1-5, 7-11, and 21-23 stand rejected under 35 U.S.C. §102(b) as being anticipated by Calof et al., Neuron 3:315-327, 1989 (hereafter "Calof"). This rejection has been overcome by amendment of the rejected claims, as described below.

The rejected claims now recite "isolated multipotent precursor cells from an olfactory epithelium of a mammal." The term "isolated" refers to the fact that cell types other than the precursor cells have been removed (see, for example, page 16, lines 14-16, and page 20, lines 8-9, of the specification). A cell is "multipotent" if "it has the potential to differentiate to form more than one type of tissue cell" (page 3, lines 24-25 of the specification). The isolated precursor cells of the present invention are multipotent, as shown by the observation that they can produce, for example, neurons, astrocytes, and oligodendrocytes (page 18, lines 18-27 of the specification).

The Examiner states that Calof discloses isolated precursor cells from the mouse olfactory epithelium. The claims have been amended to recite that the precursor cells are

multipotent. Calof does not describe isolated multipotent precursor cells. As clearly shown in Figure 7 of Calof (page 123), the basal cells produce only neuronal precursor cells, and the neuronal precursor cells produce only olfactory receptor neurons. Thus the basal cell and the neuronal precursor cell, unlike the multipotent cells described by the Applicants, are unipotent.

As Calof does not describe isolated multipotent precursor cells, as required in the amended claims, the rejection in view of Calof should be withdrawn.

#### <u>Mayo</u>

Claims 24-30 stand rejected under 35 U.S.C. §102(b) as being anticipated by Mayo et al., Int. J. Dev. Biol. 36:255-263, 1992 (hereafter "Mayo"). This rejection has been overcome by amendment of the claims to recite that the isolated precursor cells are multipotent.

The Examiner states that Mayo describes isolated precursor cells from a mouse tongue. Claim 24, as amended, recites "isolated multipotent precursor cells from a tongue of a mammal." Again, cells other than the precursor cells claimed in the present application have been removed (page 32, lines 8-17 of the specification). At no time does Mayo describe or suggest the isolation of any precursor cell population from a tongue (i.e., removal of cells other than precursor cells), let alone isolation of multipotent precursor cells. The greatest percentage of any one cell type described by Mayo is

"nearly 50%" (see Mayo, page 259, second column, line 16) after nine days in culture.

At no time does Mayo mention the presence of even one precursor cell (defined at page 7, lines 18-20, of the specification as being "neural stem cells or neural progenitor cells"). As Mayo does not disclose or suggest isolated multipotent precursor cells from a tongue, this rejection should be withdrawn.

## Rejections under 35 U.S.C. § 103(a)

Claim 6 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Calof in view of Le Gal La Salle et al., Science 259:988-990, 1993 (hereafter "Le Gal La Salle"). This rejection has been overcome by the amendment of claim 1, from which claim 6 depends, as discussed below.

Claim 6 is directed to isolated multipotent precursor cells from an olfactory epithelium of a mammal that have been transfected with a heterologous gene.

If one were to combine the teachings of Calof with those of Le Gal La Salle, one would still not have Applicants' invention.

According to the Examiner, Le Gal La Salle describes infecting primary cultures of sympathetic neurons with an adenovirus encoding  $\beta$ -galactosidase. Le Gal La Salle does not describe isolated multipotent neural precursor cells from an olfactory epithelium of a mammal.

The Examiner is referred to the above discussion of Calof in which it is pointed

out that Calof does not describe isolated multipotent precursor cells from an olfactory epithelium of a mammal.

As each reference fails to describe a central feature of the claim, namely isolated multipotent precursor cells from an olfactory epithelium of a mammal, it follows that the combination of Calof and Le Gal La Salle could not make Applicants' invention obvious. Thus, the rejection of claim 6 for obviousness should be withdrawn.

#### Conclusion

Applicants hereby submit that the claims are now in condition for allowance, and such action is respectfully requested. If the claims are not deemed to be in condition for allowance, the undersigned requests a second telephone interview in order to discuss the remaining rejections. If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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